NATIONAL TURKEY FEDERATION

JOHN O'CARROLL, *Chairman*
PETE ROTHFORK, *Vice Chairman*
JEFF ETTINGER, *Secretary-Treasurer*
BOB WRIGHT, *Immediate Past Chairman*
ALICE L. JOHNSON, DVM, *President*

February 22, 2005

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Reference: Docket No. 2004N-0479, Draft Risk Assessment of Streptogramin Resistance in *Enterococcus faecium* Attributable to the Use of Streptogramins in Animals

Dear Sir or Madam:

The National Turkey Federation is submitting the following comments on Docket Number 2004N-0479, Draft Risk Assessment of Streptogramin Resistance in *Enterococcus faecium* Attributable to the Use of Streptogramins in Animals.

The National Turkey Federation is the advocate for all segments of the U.S. turkey industry, providing services and conducting activities, which increase demand for its members' products and protect and enhance the ability to effectively and profitably provide wholesome, high quality, and nutritious turkey products.

Overall, we are encouraged by the comprehensive quantitative risk assessment undertaken by the Food and Drug Administration (agency). Due to the complexity and the utmost importance of this issue, it is imperative that such a measure is utilized to appropriately assess the perceived risks. Although we are buoyant, the draft risk assessment does have its inherent fallacies that should be addressed in preparing the final documents.

Despite the overall high standard of this draft, the final report would benefit from the correction of a number of omissions and amendments

The issue under investigation is very specific: Does the use of virginiamycin in animals present a danger to humans through the transfer of streptogramin resistance factors to *Enterococcus faecium* in humans thereby causing subsequent quinupristin-dalfopristin (Synercid®) treatment failure of *E faecium* infection. The risk assessment determined that there was no evidence for transfer of such resistance factors and accordingly was unable to formally define any risk to human health arising from virginiamycin use in animals, despite the use of two hypothetical risk attribution rates (10% and 100%) for the food pathway.

The report explains that the use of the attribution numbers was at the directive of the CVM. The report comprehensively demonstrates there is no realistic basis for the use of the 100% attribution. This attribution rate is uncorroborated by Cox and Popken, 2004[1]. These authors

[1] Cox, L.A. and D. A. Popken. **2004**. Quantifying Human Health Risk from Virginiamycin Used in Chickens. *Risk Anal.* 24(1): 271-288.

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quantify the human health risk of quinupristin-dalfopristin resistant acquired from the food pathway to be at a worst-case scenario to be 12.4%.

It is stated in the executive summary,

> *It is difficult to assess the extent of transfer of streptogramin resistance from virginiamycin-exposed E. faecium to E. faecium found in human infections based on the available data. Literature reports demonstrate that there are differences in the characteristics of resistant E. faecium isolated from animal and human sources, with respect to minimum inhibitory concentration (MIC) distributions and the presence of known resistance genes. These two findings, along with the current incomplete knowledge of the genetic basis of streptogramin resistance, prevents the risk assessment from making firm conclusions as to whether, and, if so, how much, the use of streptogramins in food animals contributes to the occurrence of streptogramin-resistant E. faecium infections in humans via a foodborne pathway.*

Nonetheless, with the summary as such, the draft report maintains the 100% attribution rate. Because the 100% attribution is unrealistic, the calculations and subsequent discussions should be deleted from the final report as it provides headline numbers, which are unfounded and are likely to be misused and misquoted in the future.

The report focuses on the role of Synercid® in the treatment of human VRE (vancomcyin resistant enterococcus) infection, but fails to account for the use of other therapies, such as linezolid. Linzolid is a relatively new antibiotic and would generally be the preferred to Synercid®. Any calculations relating to the importance of Synercid® should account for it's true use in VRE therapy, not what the usage may be if other drugs, including linezolid, were discounted. Also, the report utilizes Synercid® prescribing (usage) data which is quite aged. The final report should reflect contemporary usage rates, which are considerably lower than those presented. There is no basis for persisting with outdated data.

In Closing

In general, we applaud the FDA for utilizing a stringent quantitative risk assessment. The use of such stringency is necessary; however, there are various areas of vital importance, as discussed above, that should be addressed prior to finalizing the assessment.

Thank you for providing the opportunity to comment.

Sincerely,

Michael L Rybolt
Manager, Scientific and Technical Affairs

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